the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

The specific changes to the specification and the amended claims are shown on a separate set of pages attached hereto and entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this Amendment. On this set of pages, insertions are underlined and deletions are struck through.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 11 and 17-21 are rejected under 35 U.S.C. § 112, first paragraph as introducing new matter into claims 11 and 21. Specifically, the Examiner asserts that the specification does not teach 10 μM as a lower concentration limit and that inhibition can be achieved at far lower concentrations.

This ground of rejection is believed to be moot in view of Applicants amendment of claim 11. Claim 11 no longer recites a concentration of 10 μM. The present claim language focuses the invention on the more potent anti-telomerase effect achieved by maintaining a concentration of the catechin contacting the cells exhibiting telomerase activity with a higher concentration of a catechin than a concentration that can be reached by oral administration of the catechin as taught by the specification at pages 5-6, bridging paragraph, for example. The specification teaches means for topical administration such as injection at page 6, lines 19-21 of the present specification. Examples 4-6 describe induction of the telomerase inhibition by maintaining a 15 μM concentration of the catechin in the environment of the cells having telomerase activity.

Thus the present claim language is clearly supported by the specification which teaches maintaining a relatively high catechin concentration over an area to be treated and that topical administration can be used. In general, it was well known to those skilled in the art at the time of the claimed invention that topical administration can achieve a higher concentration in a specified area to be treated than an oral administration. Means to provide topical administration are set forth in new claim 25 which is clearly supported by the specification at page 6, lines 19-21.

In view of Applicants' amendment and arguments, withdrawal of this ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 11, and 17-20 are rejected under 35 U.S.C. § 102(b) as anticipated by JP 4264027.

The Examiner asserts that the cited reference teaches catechins obtained from green tea extracts to prevent development of colon cancer. The reference teaches that the catechins were purified from green tea to 93% purity and that the preferred concentration of catechins was 0.05 - 0.7%.

In order to have anticipation, all of the elements of the claimed invention must be taught by the cited reference. The present claims as amended are not anticipated by the cited reference.

In support of their position, Applicants submit herewith a verified translation of the cited reference JP 4264027 (Attachment A). The cited reference does not teach maintaining "a concentration of the catechin contacting the cells higher than a concentration which can be reached by oral administration of the catechin" as presently claimed. The disclosure of JP 4264027 is drawn solely to oral administration of polyphenols, preferably in the form of foods (see paragraph 0010 of the translation, for example). Also JP 4264027 teaches administration of much lower levels of polyphenols than the levels claimed by Applicants. Thus, the advantages of higher concentrations of catechins (as discussed on pages 5-6, bridging paragraph of the present specification) are not taught by the cited reference and cannot be achieved by practice of the teaching therein.

As the English abstract of JP 4264027 describes, the composition for prevention of colon cancer taught by the cited reference comprises polyphenols represented by the formula (1) and/or (2) and that the content of the polyphenol component is 0.05-0.7%. The polyphenols are e.g. (+) catechin, (-) epicatechin, (+) gallocatechin, (-) epigallocatechin, (-) epicatechin gallate, and (-) epigallocatechin gallate.

The administration form of the composition taught by JP 4264027 is preferably in the form of foods, including various confectioneries and beverages at an amount of 0.05-0.7% (see paragraph 0010). JP 4260427 does not teach administration of the polyphenol composition except as a food additive.

In contrast, Applicants' claimed invention is drawn to administration of a dosage form suitable for parenteral administration. The present specification at page 6, lines 17-21 teaches pharmaceutical compositions including injections and plasters, which are suitable to achieve high

catechin concentrations such as 15 μM as taught in Examples 4 and 5 of the present specification. Parenteral administration is particularly defined in new claims 24 and 25. Thus, Applicants' claimed invention differs from the cited reference both in the mode of administration and in the levels of catechin administered.

Claim 23, newly presented, claims effective concentrations including 15 μM. Such concentrations are not disclosed in the JP 4264027 document as discussed below.

Test Example 1 of JP 4264027 describes Fisher rats that were allowed to take (a) water to drink containing 0.01% of tea polyphenols or (b) a powder feed containing 0.015% of tea polyphenols for 16 weeks between the 11th and 26th week. Neither treatment provides for a concentration of catechin contacting the cells higher than a concentration which can be reached by oral administration of the catechin or an effective concentration of about 15 μM in view of the two publications presented below (Attachments B & C).

Kim et al. (Attachment B) teaches that when Sprague-Dawley rats drank water containing 0.6% green tea polyphenol preparation for four weeks, the plasma concentrations of EGCg, EGC, and EC were in the range between 200 to 400 ng/ml, respectively (see Figures 2 and 3 on page 44 of Attachment B). The highest value (1000 ng/ml for EGC and EC) was obtained in the second week. In contrast, Applicants' claimed level of 15 μM translates to a plasma concentration of 6875 ng/ml, clearly much higher than the concentration taught by JP 4264027. Since the concentrations as claimed by Applicants are not taught by the cited reference, JP 4264027 does not anticipate the present claims.

JP 4264027 teaches that an effective amount of polyphenols is 300-600 mg/day (paragraph 0017). Chow et al (Attachment C) teaches that the largest value of plasma concentration of EGCg within 24 hours was about 400 ng/ml by administration of EGCg to the volunteers at 200, 400, 600 and 800 mg (see Figure 1 on page 55). This data further supports Applicants' position that the polyphenol levels taught by JP 4264027 do not anticipate Applicants' claims.

JP 4264027 does not teach parenteral administration and the oral administration of polyphenols described in JP 4264027 does not achieve the concentration ranges claimed by Applicants. Consequently, JP 4264027 cannot anticipate Applicants' claims.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: May 1, 2002

By: Che S. Chereskin

Che Swyden Chereskin
Registration No. 41,466
Agent of Record
620 Newport Center Drive
Sixteenth Floor
Newport Beach, CA 92660
(949) 760-0404

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 11 and 20 have been amended as follows:

11. (Four times amended) A method of inhibiting telomerase activity comprising a step of contacting cells exhibiting telomerase activity with a telomerase inhibitor comprising a catechin ~~at a concentration of at least 10 μM~~to maintain a concentration of the catechin contacting the cells higher than a concentration which can be reached by oral administration of the catechin.

17. The method according to Claim 11, wherein the telomerase inhibitor comprises a green tea extract containing a catechin.

18. The method according to Claim 11, wherein the catechin is epigallocatechin gallate, epigallocatechin, epicatechin gallate, or epicatechin.

19. The method according to Claim 11, wherein the telomerase inhibitor further comprises pharmaceutically acceptable carrier or diluent.

20. (Amended) The method according to Claim 11, wherein the telomerase inhibitor ~~comprise~~ comprises the catechin in an amount of 90 to 95% by weight.

21. A method according to claim 17, wherein the green tea extract contains epigallocatechin gallate in an amount of at least 10 wt%.